

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/GB2005/000497

International filing date (day/month/year)  
11.02.2005

Priority date (day/month/year)  
12.02.2004

International Patent Classification (IPC) or both national classification and IPC  
A61K31/496, A61K31/506, A61P21/00, C07D239/48

Applicant  
VERNALIS (R&D) LTD.

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material:  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing:  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 27-40,42

because:

☒ the said international application, or the said claims Nos. 27-40,42 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/GB2005/000497

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**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-42
	No: Claims	
Inventive step (IS)	Yes: Claims	1-42
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-26,41
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

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**Box No. VI Certain documents cited**

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**1. Certain published documents (Rules 43bis.1 and 70.10)**

**and / or**

**2. Non-written disclosures (Rules 43bis.1 and 70.9)**

**see form 210**

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**Box No. VII Certain defects in the international application**

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The following defects in the form or contents of the international application have been noted:

**see separate sheet**

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**Box No. VIII Certain observations on the international application**

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The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

The following documents (D) are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

- D1: WO 2004/080979 A (LG LIFE SCIENCES LTD; LEE, JINHO; KIM, HAK JOONG; CHOI, SEIHYUN; CHOI,) 23 September 2004 (2004-09-23)
- D2: WO 2004/029204 A (MERCK & CO., INC; KOPKA, IHOR, E; LI, BING; HAGMANN, WILLIAM, K) 8 April 2004 (2004-04-08)
- D3: WO 02/055084 A (VERNALIS RESEARCH LIMITED; GILLESPIE, ROGER, JOHN; LERPINIÈRE, JOANNE) 18 July 2002 (2002-07-18)
- D4: SAKAMOTO, T.; ET AL.: CHEM. PHARM. BULL., vol. 28, no. 2, 1980, pages 571-577, XP001206934
- D5: SAKAMOTO, T.; ET AL.: CHEM. PHARM. BULL., vol. 28, no. 1, 1980, pages 202-207, XP001206935
- D6: OBRECHT D ET AL: "5. A NOVEL AND EFFICIENT APPROACH FOR THE COMBINATORIAL SYNTHESIS OF STRUCTURALLY DIVERSE PYRIMIDINES ON SOLID SUPPORT" HELVETICA CHIMICA ACTA, VERLAG HELVETICA CHIMICA ACTA. BASEL, CH, vol. 80, 1997, pages 65-72, XP002915327 ISSN: 0018-019X

The present application relates to pyrimidine compounds as purine receptor antagonists.

### item III

For the assessment of the present claims 27-40 and 42 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.



WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)

International application No.

PCT/GB2005/000497

## item V

1. Novelty (Art. 33(2) PCT)

Compounds according to product-claim 23 differ from compounds disclosed in the cited prior art in the basic structure (D3: general formula (I)) or at least a different substituent  $R_2$  (D4: examples VIIIa-c, Ph; D5: examples VIa, VIc, Ph; D6: examples 10-12, MeOPh). The use of compounds of general formula (I) of present claim 1 is not disclosed in the cited documents either. The presently claimed subject-matter is thus considered novel within the meaning of Art. 33(2) PCT.

2. Inventive step (Art. 33(3) PCT)

Document D3 relates to pyrrolo[2,3-d]pyrimidine derivatives and their use as purinergic receptor antagonists for the treatment of Parkinson's disease. It is considered most relevant state of the art. The problem to be solved by the present application can be seen as to provide further compounds for the same use. Due to the structural differences between the claimed compounds and those disclosed in D3, it cannot be considered obvious for the skilled person to provide compounds according to present claim 23 or the use according to present claim 1 when starting from the technical teaching disclosed in D3. The presence of an inventive step can thus be acknowledged for the present claims.

3. Industrial applicability (Art. 33(4) PCT)

Can be acknowledged for claims 1-26 and 41.

## item VI

Documents D1 and D2 were published after the priority date of the present application but before its international filing date. Their content would be considered as forming part

of the state of the art if the priority of the present application was found to be invalid.

**item VII**

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in documents D3 is not mentioned in the description, nor is this document identified therein.

**item VIII**

1. The expression "prodrug" used in several claims does not have a precise meaning in the art. The skilled person is thus not in the position to determine the exact scope of protection which should, however, be clearly and unambiguously defined by the claims (Art. 6 PCT). The skilled person is furthermore not in a position to perform the alleged invention since there is no clear teaching in the application documents on file which indicates how to carry out the alleged invention without undue burden, i.e. the disclosure is considered insufficient within the meaning of Art. 5 PCT.
2. Reference to the description (claim 24) is not allowable with respect to clarity of the claims (Art. 6 PCT).